```
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09980593.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 09:32:16 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   4520 TO ITERATE

 22.1% PROCESSED    1000 ITERATIONS                                0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        86370 TO    94430
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 09:32:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  91344 TO ITERATE

100.0% PROCESSED   91344 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.03

L3            0 SEA SSS FUL L1

=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              148.55     148.76

STN INTERNATIONAL LOGOFF AT 09:32:43 ON 19 MAR 2003
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Broad search

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09980593.str

L1 STRUCTURE UPLOADED

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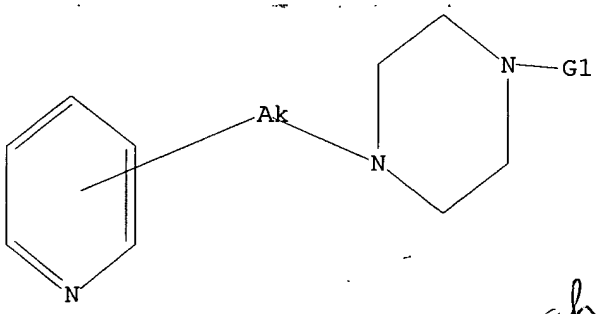
L1 HAS NO ANSWERS
L1 STR



G1 C,SO2
G2 C,N

search also submitted to library

Structure attributes mus reparation.

=> s l1
SAMPLE SEARCH INITIATED 0
SAMPLE SCREEN SEARCH COMPI

15.2% PROCESSED 1000 I 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM I
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLI
BATC LETE**
PROJECTED ITERATIONS: 126681 TO 136399
PROJECTED ANSWERS: 3339 TO 5079

L2 32 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 09:40:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 131073 TO ITERATE

100.0% PROCESSED 131073 ITERATIONS 3286 ANSWERS
SEARCH TIME: 00.00.03

L3 3286 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.15	148.36

FILE 'CAPLUS' ENTERED AT 09:40:54 ON 19 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Mar 2003 VOL 138 ISS 12
FILE LAST UPDATED: 18 Mar 2003 (20030318/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 1884 L3

=> s l4 and metalloprotein?
L5 15 L4 AND METALLOPROTEIN?

=> d ibib abs hitstr tot

L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:5956 CAPLUS
DOCUMENT NUMBER: 138:73254
TITLE: Preparation of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses
INVENTOR(S): Bilodeau, Mark T.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

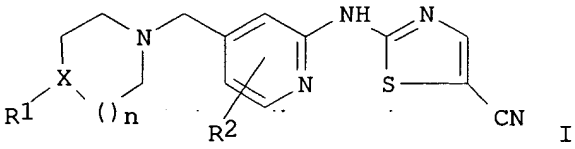
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000687	A1	20030103	WO 2002-US21110	20020618

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-300245P P 20010622
OTHER SOURCE(S): MARPAT 138:73254

GI



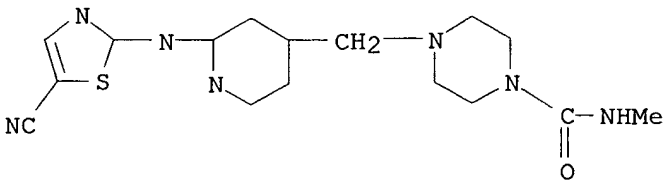
I

AB The present invention relates to thiazolylaminopyridines (shown as I; variables defined below; e.g. 4-[2-(5-cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide) which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compns. which contain these compds., and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammatory diseases, and the like in mammals. For I: n is 0 or 1; X is C-H or N, provided X is C-H if n = 1 and R1 is SO2-(C1-C6 alkyl) and provided that X is C-H if R1 is NH(C:O)NR3H; R1 is SO2(C1-C6 alkyl), (C:O)NR3H, or NH(C:O)NR3H; R2 is H, OH, OC1-C6 alkyl, C1-C6 alkyl, or halo; and R3 is C1-C6 alkyl. Compds. I inhibit VEGF-stimulated mitogenesis of human vascular endothelial cells in culture with IC50 values = 0.01-5.0 .mu.M. 4-[2-(5-Cyanothiazol-2-ylamino)pyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide, 2-[[4-[[4-(methylsulfonyl)piperidin-1-yl]methyl]pyridin-2-yl]amino]-1,3-thiazole-5-carbonitrile, and 4-[2-(5-cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide show enhanced pharmacokinetic properties as compared to previously reported thiazolylaminopyridines in WO 01/17995 A1. Although the methods of prepn. are not claimed, 13 example prepns. are included.

IT **479611-82-0P**, 4-[[2-(5-Cyanothiazol-2-ylamino)pyridin-4-yl]methyl]piperazine-1-carboxylic acid methylamide **479612-56-1P**, 4-[2-(5-Cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide trifluoroacetate
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses)

RN 479611-82-0 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



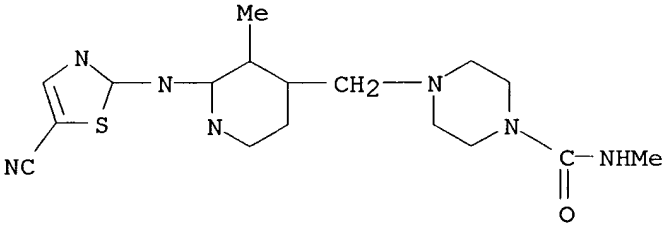
*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 479612-56-1 CAPLUS

CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-3-methyl-4-pyridinyl]methyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

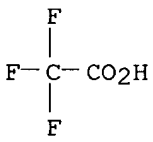
CRN 479612-55-0
CMF C17 H21 N7 O S



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

CM 2

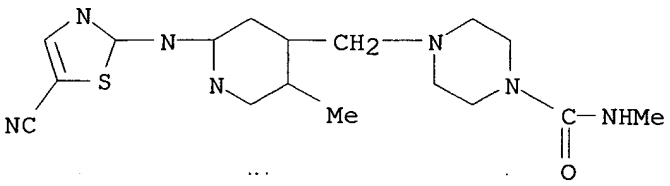
CRN 76-05-1
CMF C2 H F3 O2



IT **479612-28-7P**, 4-[2-(5-Cyanothiazol-2-ylamino)-5-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide **479612-29-8P**, 4-[[2-(5-Cyanothiazol-2-ylamino)-5-methylpyridin-4-yl]methyl]piperazine-1-carboxylic acid methylamide trifluoroacetate **479612-55-0P**, 4-[2-(5-Cyanothiazol-2-ylamino)-3-methylpyridin-4-ylmethyl]piperazine-1-carboxylic acid methylamide **479612-74-3P**, 4-[[2-Chloro-6-[(5-cyano-1,3-thiazol-2-yl)amino]pyridin-4-yl]methyl]-N-methylpiperazine-1-carboxamide **479612-92-5P**, 4-[[2-[(5-Cyano-1,3-thiazol-2-yl)amino]-6-ethylpyridin-4-yl]methyl]-N-methylpiperazine-1-carboxamide **479613-12-2P**, 2-[[4-[(4-Acetylpiperazin-1-yl)methyl]-6-methylpyridin-2-yl]amino]-1,3-thiazole-5-carbonitrile **479613-13-3P**, 2-[[4-[(4-Acetylpiperazin-1-yl)methyl]-6-methylpyridin-2-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses)

RN 479612-28-7 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-5-methyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)

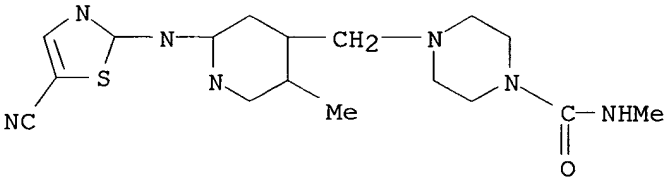


*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 479612-29-8 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-5-methyl-4-pyridinyl]methyl]-N-methyl-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

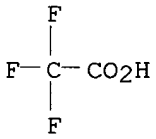
CRN 479612-28-7
CMF C17 H21 N7 O S



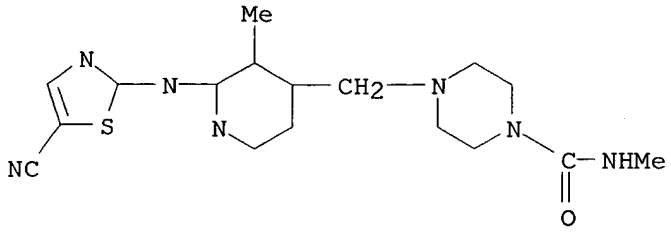
*** FRAGMENT DIAGRAM IS INCOMPLETE ***

CM 2

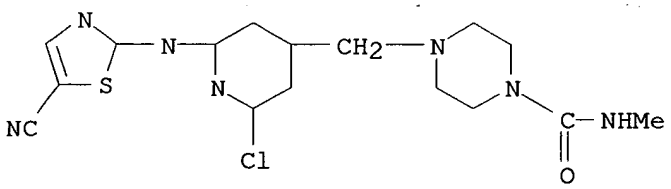
CRN 76-05-1
CMF C2 H F3 O2



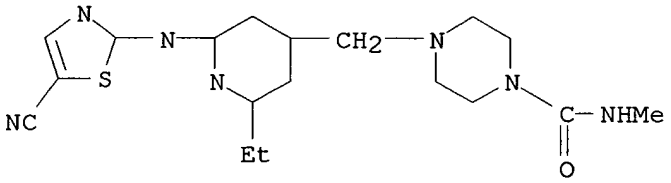
RN 479612-55-0 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-3-methyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



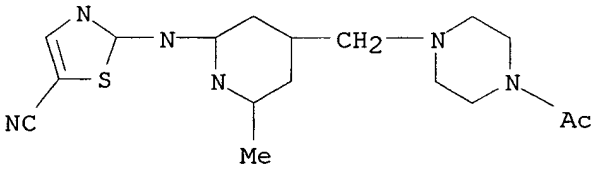
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 479612-74-3 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-chloro-6-[(5-cyano-2-thiazolyl)amino]-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 479612-92-5 CAPLUS
CN 1-Piperazinecarboxamide, 4-[[2-[(5-cyano-2-thiazolyl)amino]-6-ethyl-4-pyridinyl]methyl]-N-methyl- (9CI) (CA INDEX NAME)



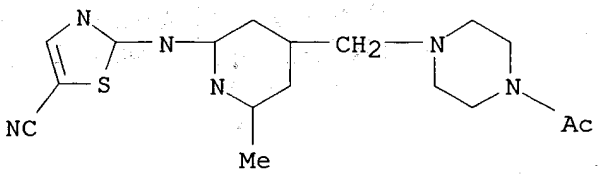
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 479613-12-2 CAPLUS
CN Piperazine, 1-acetyl-4-[[2-[(5-cyano-2-thiazolyl)amino]-6-methyl-4-pyridinyl]methyl]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***
RN 479613-13-3 CAPLUS
CN Piperazine, 1-acetyl-4-[[2-[(5-cyano-2-thiazolyl)amino]-6-methyl-4-pyridinyl]methyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

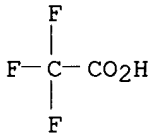
CRN 479613-12-2
CMF C17 H20 N6 O S



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

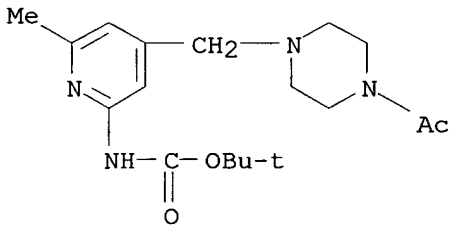
CM 2

CRN 76-05-1
CMF C2 H F3 O2

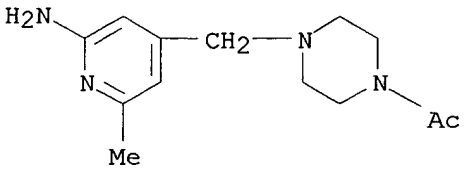


IT **479613-21-3P**, tert-Butyl 4-[(4-acetylpiperazin-1-yl)methyl]-6-methylpyridin-2-ylcarbamate **479613-27-9P**, 1-Acetyl-4-[(2-amino-6-methylpyridin-4-yl)methyl]piperazin-4-ium chloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of thiazolylaminopyridines as tyrosine kinase inhibitors with therapeutic uses)

RN 479613-21-3 CAPLUS
CN Carbamic acid, [4-[(4-acetyl-1-piperazinyl)methyl]-6-methyl-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 479613-27-9 CAPLUS
CN Piperazine, 1-acetyl-4-[(2-amino-6-methyl-4-pyridinyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:849621 CAPLUS
DOCUMENT NUMBER: 137:353056
TITLE: Preparation of benzenesulfonylpiperazines as matrix **metalloproteinase** inhibitors.
INVENTOR(S): Chung, Yong-Jun; Lee, Keyong-Ho; Kim, Youn-Chul; Park, Ho-Jin
PATENT ASSIGNEE(S): Kolon Ind. Inc., S. Korea
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088115	A1	20021107	WO 2002-KR759	20020424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
KR 2001-22767 A 20010426
KR 2001-77522 A 20011207
KR 2002-14481 A 20020318

OTHER SOURCE(S): MARPAT 137:353056
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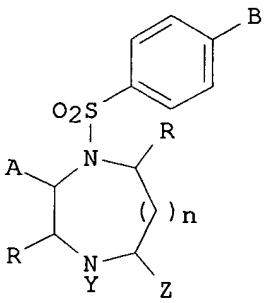


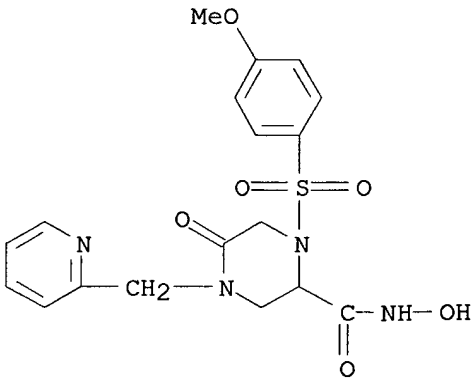
I

AB Title compds. [I; n = 0-3; A = CO2H, CONHOH, CH2SH, CH2OH; B = H, alkyl, NO2, aryl, heteroaryl, pyrrolyl, halo, alkoxy, aryloxy, alkylamino, alkylthio, CONHR, NHCOR, NHCO2R, NHCONHR, etc.; R = H, alkyl, aryl, heteroaryl, tetragonal to octagonal cyclic compd., alkyl substituted by a tetragonal to octagonal (hetero)cyclic compd.; Z = H, O, S, provided that when Z = O, S it takes a double bond; Y = H, alkyl, aryl, heteroaryl, alkyl substituted by a tetragonal to octagonal cyclic compd., alkyl substituted by a tetragonal to octagonal heterocyclyl, CONHR, NHCOR, NHCO2R, NHCONHR, alkyl having a double or triple bond], were prepd. Thus, Me 1-(4-methoxybenzenesulfonyl)-5-oxopiperazine-2-carboxylate (prepn. given) was stirred 5 h with aq. NH2OH to give 45% 1-(4-methoxybenzenesulfonyl)-5-oxopiperazine-2-hydroxamic acid. This inhibited MMP-2 with IC50 = 0.004 .mu.M. I are angiogenesis controlling materials that can inhibit overexpression of matrix **metalloproteinase** that decomps. protein constituents in extracellular matrix and basement membranes of connective tissues.

IT **474410-22-5P 474410-24-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzenesulfonylpiperazines as matrix **metalloproteinase** inhibitors)

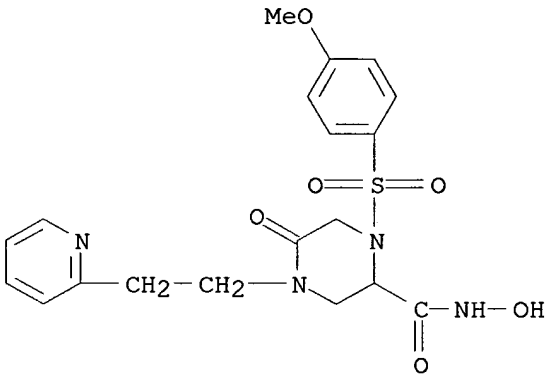
RN 474410-22-5 CAPLUS

CN 2-Piperazinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-5-oxo-4-(2-pyridinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

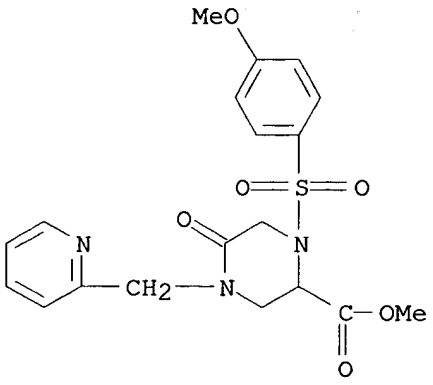


● HCl

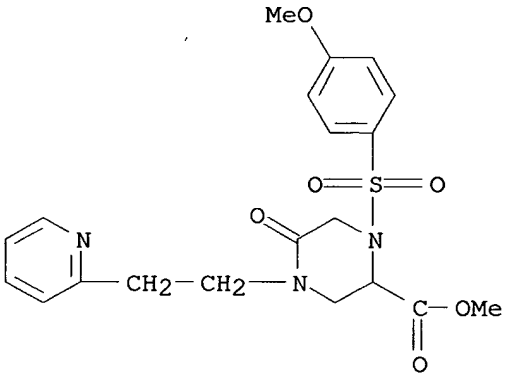
RN 474410-24-7 CAPLUS
CN 2-Piperazinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-5-oxo-4-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



IT **474410-45-2P 474410-46-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of benzenesulfonylpiperazines as matrix **metalloproteinase** inhibitors)
RN 474410-45-2 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-4-(2-pyridinylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 474410-46-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-[(4-methoxyphenyl)sulfonyl]-5-oxo-4-[2-(2-pyridinyl)ethyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:849440 CAPLUS
DOCUMENT NUMBER: 137:333179
TITLE: Use of HIV protease inhibitors to block cell migration and/or invasion, tissue infiltration, and edema, and therapeutic use
INVENTOR(S): Ensoli, Barbara
PATENT ASSIGNEE(S): Istituto Superiore di Sanita', Italy
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002087583	A2	20021107	WO 2002-EP4303	20020418
WO 2002087583	A3	20021219		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2001-RM210 A 20010418

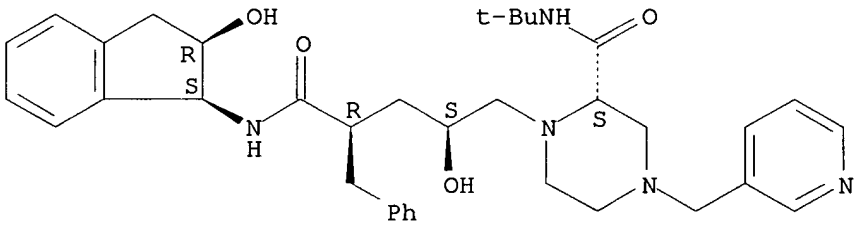
AB The invention provides a method using HIV protease inhibitors for blocking the invasion of normal, neoplastic, inflammatory, or immune cells, tissue infiltration, and/or edema formation through inhibition or modulation of mols. and proteolytic enzymes (e.g. matrix **metalloproteinases**), for the therapy of diseases whose pathogenesis is related to the above processes, including tumors, non-neoplastic angioproliferative diseases, inflammatory diseases, or autoimmune diseases.

IT **150378-17-9**, Indinavir **150378-17-9D**, Indinavir, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV protease inhibitors to block cell migration and/or invasion, tissue infiltration, and edema, and therapeutic use)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

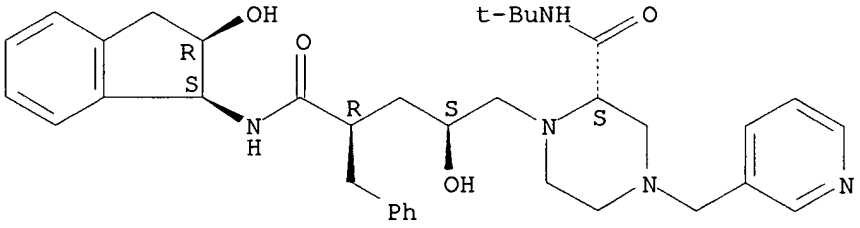
Absolute stereochemistry.



RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:638144 CAPLUS
DOCUMENT NUMBER: 137:163841
TITLE: Methods for regulating levels of zinc, cadmium, and calcium in humans and for diagnosing, or screening for the risk of developing diseases associated with abnormal levels of cadmium, zinc and calcium in body fluids and tissues
INVENTOR(S): Woods, Gordon L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S. Ser. No. 610,538, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002114848	A1	20020822	US 2001-989674	20011121
PRIORITY APPLN. INFO.:			US 1999-142926P P	19990709
			US 2000-610538 B2	20000707

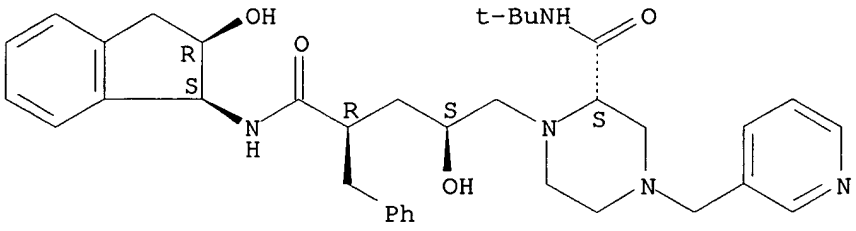
AB Methods and compns. are provided for decreasing PGE2:PGF2.alpha., regulating ratios of zinc:cadmium and regulating the concn. of zinc, calcium and zinc-contg. and PGE2-dependent matrix **metalloproteinases** in body fluids and tissues of a human. Elevated or otherwise unregulated levels of PGE2, zinc and calcium and elevated concns. of zinc-contg. and PGE2-dependent matrix **metalloproteinases** have been found to be assocd. with the development of certain diseases. Methods for the prevention of a variety of diseases are also disclosed.

IT **157810-81-6**, Indinavir sulfate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zinc, cadmium, and calcium level regulation in humans, and use in disease diagnosis and prevention)
RN 157810-81-6 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

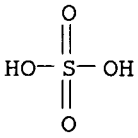
CRN 150378-17-9
CMF C36 H47 N5 O4

Absolute stereochemistry.



CM 2

CRN 7664-93-9
CMF H2 O4 S



L5 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:521462 CAPLUS
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053138	A2	20020711	WO 2002-IE1	20020102
WO 2002053138	A3	20020919		

W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IE 2001-2 A 20010102
OTHER SOURCE(S): MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immundysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixt. showed antitumor activity against various human carcinomas and melanomas and antimicrobial

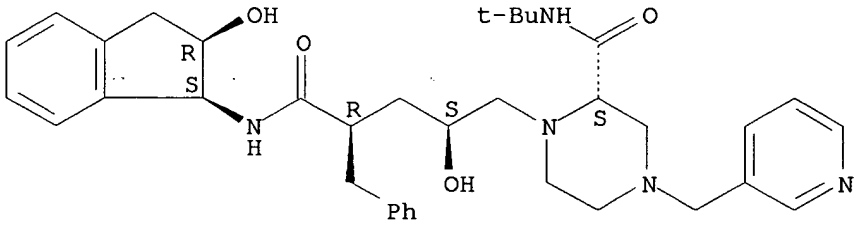
activity against Staphylococcus aureus and Enterococcus faecalis.

IT **150378-17-9,** Indinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further contg.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:223957 CAPLUS

DOCUMENT NUMBER: 137:88006

TITLE: HIV protease inhibitors are potent anti-angiogenic molecules and promote regression of Kaposi sarcoma

AUTHOR(S): Sgadari, Cecilia; Barillari, Giovanni; Toschi, Elena; Carlei, Davide; Bacigalupo, Ilaria; Baccarini, Sara; Palladino, Clelia; Leone, Patrizia; Bugarini, Roberto; Malavasi, Laura; Cafaro, Aurelio; Falchi, Mario; Valdembri, Donatella; Rezza, S, Giovanni; Bussolino, Federico; Monini, Paolo; Ensoli, Barbara

CORPORATE SOURCE: Laboratory of Virology, Istituto Superiore di Sanita, Rome, Italy

SOURCE: Nature Medicine (New York, NY, United States) (2002), 8(3), 225-232
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature America Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Treatment with HIV-1 protease inhibitors (PI) is assocd. with a reduced incidence or regression of Kaposi sarcoma (KS). Here we show that systemic administration of the Pls indinavir or saquinavir to nude mice blocks the development and induces regression of angioproliferative KS-like lesions promoted by primary human KS cells, basic fibroblast growth factor (bFGF), or bFGF and vascular endothelial growth factor (VEGF) combined. These PIs also block bFGF or VEGF-induced angiogenesis in the chorioallantoic membrane assay with a potency similar to paclitaxel (Taxol). These effects are mediated by the inhibition of endothelial- and KS-cell invasion and of matrix **metalloproteinase**-2 proteolytic activation by Pis at concns. present in plasma of treated individuals. As PIs also inhibit the in vivo growth and invasion of an angiogenic tumor-cell line, these data indicate that Pis are potent anti-angiogenic and anti-tumor mols. that might be used in treating non-HIV KS and in

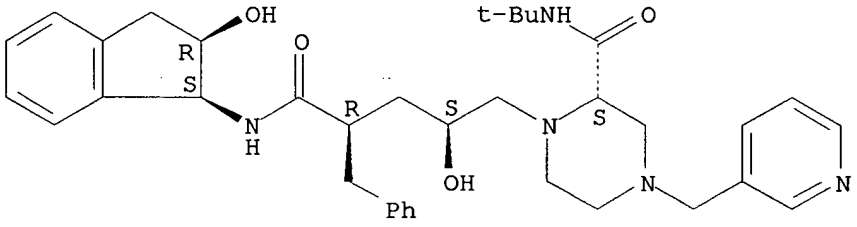
other HIV-assocd. tumors.

IT **150378-17-9**, Indinavir
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV protease inhibitors are potent anti-angiogenic mols. and promote regression of Kaposi sarcoma)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:46330 CAPLUS

DOCUMENT NUMBER: 137:134505

TITLE: Synergistic antiadipogenic effects of HIV type 1 protease inhibitors with tumor necrosis factor .alpha.: Suppression of extracellular insulin action mediated by extracellular matrix-degrading proteases

AUTHOR(S): Mondal, Debasis; Larussa, Vincent F.; Agrawal, Krishna C.

CORPORATE SOURCE: Department of Pharmacology, Tulane University School of Medicine, New Orleans, LA, 70112, USA

SOURCE: AIDS Research and Human Retroviruses (2001), 17(17), 1569-1584
CODEN: ARHRE7; ISSN: 0889-2229

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Long-term use of HIV-1 protease inhibitors (PIs) is assocd. with a lipodystrophy syndrome. To delineate the assocd. mechanisms, adipogenesis was detd. in 3T3-L1 cells in the presence or absence of either indinavir (2-50 .mu.g/mL) or ritonavir (0.4-10 .mu.g/mL). A concn.-dependent decrease in both lipid (4-59%) and triglyceride (11-49%) levels was seen after 10 days of exposure. Simultaneous treatment with TNF-.alpha. showed a synergistic suppression in lipid levels by 45-95% at 10 U/mL and almost complete suppression at 100 U/mL. The effect of PIs on insulin-induced lipogenesis was monitored by [14C]glucose incorporation into lipids, which was suppressed by 21-86% in a concn.-dependent manner. Insulin-sensitizing agent, troglitazone (80 and 400 nM), effectively blocked the PI-mediated adipogenic suppression. Preadipocyte factor 1 gene (pref-1) expression, as monitored by RT-PCR, was down-regulated (4- to 6-fold) within 48 h after insulin stimulation; however, a smaller

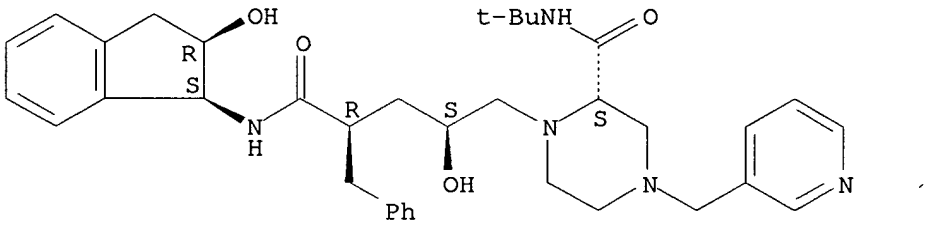
decrease (1.2- to 1.8-fold) was obsd. in PI-exposed cells. The decrease in proteolytic activity of matrix metalloproteases (MMP-2 and MMP-9) during adipogenesis was reversed on exposure to the PIs. Similarly, the plasminolytic activity was increased and plasminogen activator inhibitor (PAI) activity was decreased in supernatants from PI-treated cells. The insulin-mediated induction (3- to 4-fold) of PAI-1 and PAI-2 message was suppressed on exposure to PIs, which was reversed by troglitazone treatment. Thus, the HIV-1 PIs may suppress adipogenesis by disrupting the concerted actions of host proteases that regulate ECM integrity required for initiation of differentiation.

IT **150378-17-9**, Indinavir
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic antiadipogenic effects of HIV type 1 proteinase inhibitors with TNF-.alpha. with suppression of extracellular insulin action mediated by extracellular matrix-degrading proteinases)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:749723 CAPLUS
DOCUMENT NUMBER: 136:31301
TITLE: Three-Dimensional Quantitative Structure-Activity Relationship (3D-QSAR) Models for a Novel Class of Piperazine-Based Stromelysin-1 (MMP-3) Inhibitors: Applying a "Divide and Conquer" Strategy
AUTHOR(S): Amin, Elizabeth Ambrose; Welsh, William J.
CORPORATE SOURCE: Department of Chemistry & Biochemistry, University of Missouri-St. Louis, St. Louis, MO, 63121, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(23), 3849-3855
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

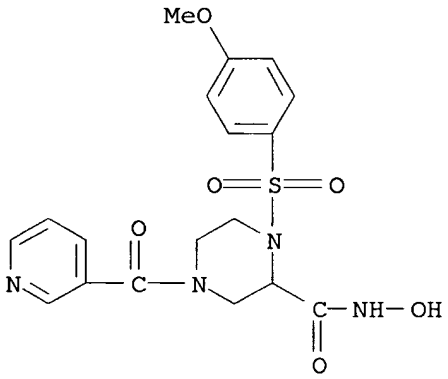
AB Three-dimensional quant. structure-activity relationship (3D-QSAR) models have been obtained using comparative mol. field anal. (CoMFA) for a novel series of piperazine-based matrix **metalloproteinase** inhibitors (MMPIs). The crystal structure of stromelysin-1 (MMP-3) was used to identify regions of the enzyme and inhibitors where steric and

electrostatic effects correlate strongly with biol. activity. A training set composed of a subset of inhibitors (#10-35), which differed only with regards to the substituent (n-alkyl, amide, carbamide and sulfonamide) on the piperazine distal nitrogen, yielded the most predictive CoMFA model, with r2 values of 0.592 (cross-validated) and 0.989 (conventional); this model was further validated using test compds. from two inhibitor subsets. Investigation of various ligand conformations, inhibitor subsets, alignment schemes and partial charge formalisms was required to obtain satisfactory models. The greatest success was achieved by incorporating inertial alignment together with manual adjustment of the enzyme-docked inhibitors to ensure complementarity between the inhibitors' substituent conformations and the structural characteristics of the MMP-3 S1-S2' binding pockets. Key insights into the structure-activity relationship (SAR) obtained from this anal. for this inhibitor set are in agreement with exptl. obsd. data on stromelysin-1 biol. activity and binding-site topol. In particular, the present study sheds new light on the steric and electrostatic requirements for ligand binding to the partly solvent-exposed S1-S2' area.

IT **262420-38-2**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three-dimensional quant. structure-activity relationship (3D-QSAR) models for a novel class of piperazine-based stromelysin-1 (MMP-3) inhibitors)

RN 262420-38-2 CAPLUS

CN 2-Piperazinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:564870 CAPLUS
DOCUMENT NUMBER: 135:132456
TITLE: Treatment of neuropsychiatric diseases with protease and neuraminidase inhibitors, and screening method
INVENTOR(S): Vawter, Marquis P.; Freed, William J.
PATENT ASSIGNEE(S): Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054729	A1	20010802	WO 2001-US2417	20010125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001031137	A5	20010807	AU 2001-31137	20010125

PRIORITY APPLN. INFO.: US 2000-177971P P 20000125
WO 2001-US2417 W 20010125

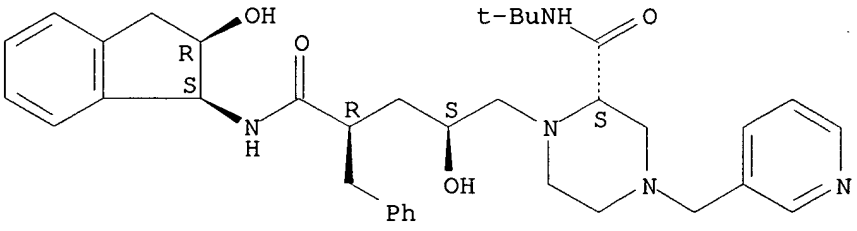
AB The invention provides a method of treating a neuropsychiatric disease characterized by an abnormally elevated level of a fragment of an isoform of a neural cell adhesion mol. (N-CAM) in the brain or cerebrospinal fluid of an affected human subject, comprising administering a therapeutically effective amt. of at least one compd. selected from protease inhibitors and neuraminidase inhibitors, whereby administering the compd. to the subject treats the human subject. The invention further provides a method of monitoring the efficacy of treatment with the method of the present invention. Moreover, the invention provides a method of screening for compds. effective in treating neuropsychiatric disease assocd. with an abnormally elevated level of a fragment of a N-CAM in the cerebrospinal fluid of an affected human subject. Further provided are fragments of an isoform of N-CAM in the cerebrospinal fluid of human subjects.

IT **150378-17-9**, Indinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protease and neuraminidase inhibitors for treatment of neuropsychiatric diseases, and screening method)

RN 150378-17-9 CAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

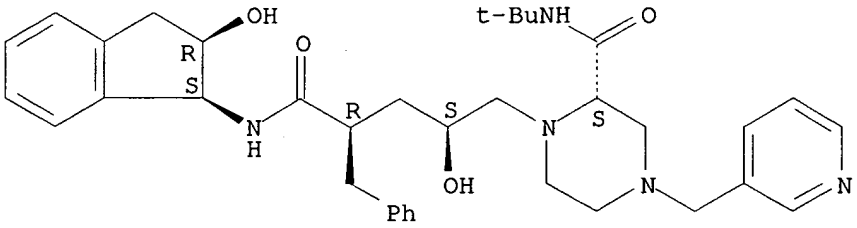
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

IT **150378-17-9**, Indinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 150378-17-9 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-

inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



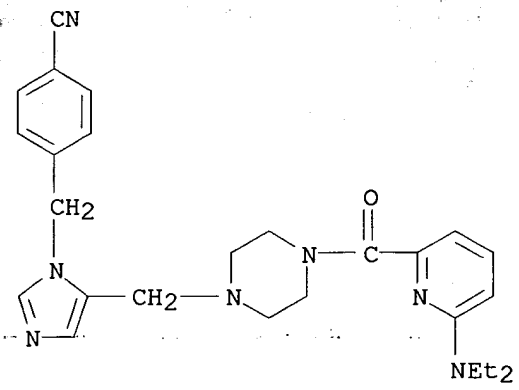
L5 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:247178 CAPLUS
DOCUMENT NUMBER: 134:275776
TITLE: Method using a geranylgeranyl-protein transferase inhibitor for preventing osteoporosis, pharmaceutical compositions, and compound preparation
INVENTOR(S): Reszka, Alfred A.; Rodan, Gideon A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022963	A1	20010405	WO 2000-US26357	20000925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-156234P P 19990927
OTHER SOURCE(S): MARPAT 134:275776
AB A method for preventing or inhibiting bone resorption in a mammal comprises administering to a mammal in need thereof a therapeutically effective amt. of an inhibitor of geranylgeranyl-protein transferase type I.
IT **290819-82-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(geranylgeranyl-protein transferase inhibitor for preventing bone resorption, pharmaceutical compns., and compd. prepn.)
RN 290819-82-8 CAPLUS
CN Piperazine, 1-[[1-[(4-cyanophenyl)methyl]-1H-imidazol-5-yl]methyl]-4-[[6-

(diethylamino)-2-pyridinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

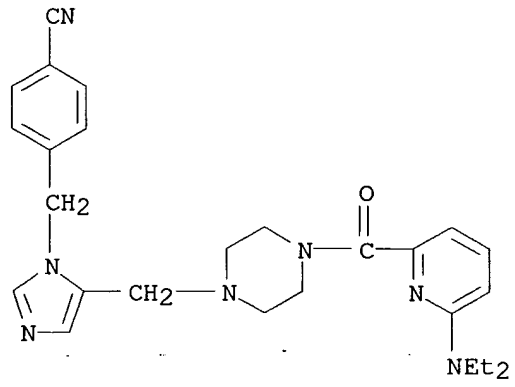


● 3 HCl

IT **290819-51-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(geranylgeranyl-protein transferase inhibitor for preventing bone resorption, pharmaceutical compns., and compd. prepn.)

RN 290819-51-1 CAPLUS

CN Piperazine, 1-[[1-[(4-cyanophenyl)methyl]-1H-imidazol-5-yl]methyl]-4-[[6-(diethylamino)-2-pyridinyl]carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:50495 CAPLUS
DOCUMENT NUMBER: 134:95488
TITLE: Cadmium containing compositions for prevention and

treatment of prostate cancer
INVENTOR(S): Woods, Gordon L.
PATENT ASSIGNEE(S): Cancer2 Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003708	A1	20010118	WO 2000-US18580	20000707
W: CA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1200104	A1	20020502	EP 2000-947094	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2002148049	A1	20021017	US 2002-38035	20020102

PRIORITY APPLN. INFO.:
US 1999-142926P P 19990709
EP 1999-113269 A 19990708
WO 2000-US18580 W 20000707

AB Methods and compns. are provided for decreasing or regulating ratios of zinc:cadmium and PGE2:PGF2.alpha. and regulating the concn. of zinc-contg. and PGE2-dependent matrix **metalloproteinases** in body fluids and tissues of a mammal, comprising administering to the mammal an amt. of a pharmaceutically acceptable and bioavailable cadmium salt. Elevated or fluctuating levels of PGE2 and zinc and elevated concns. of zinc-contg. and PGE2-dependent matrix **metalloproteinases** have been found to be assocd. with the development of certain diseases, e.g. prostate cancer, diabetes, and multiple sclerosis. Ejaculates from horse stallions showed that when the concn. of cadmium is increased, the sperm motility decreases. Motility of the sperm correlates to sperm viability which is an indicator of the proliferation environment of the stallion's prostate glands. Higher cadmium values from semen decreases the proliferation of prostate cells and replication of viruses within the prostate environment. Thus elevating the cadmium concn. in man's prostate gland will decrease man's incidence of prostate cancer, decreases his fertility, and protects against viral infections and age-onset diseases.

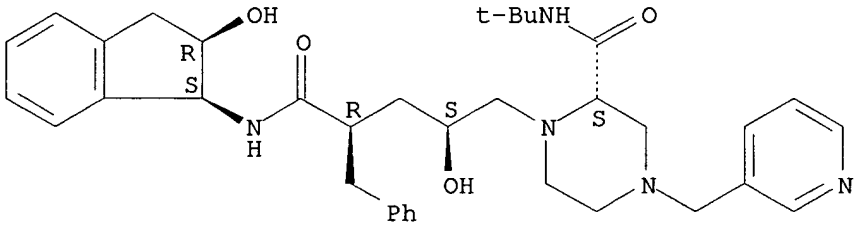
IT **157810-81-6**, Indinavir sulfate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cadmium contg. compns. for prevention and treatment of prostate cancer)

RN 157810-81-6 CAPLUS
CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)-, sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

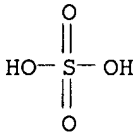
CRN 150378-17-9
CMF C36 H47 N5 O4

Absolute stereochemistry.



CM 2

CRN 7664-93-9
CMF H2 O4 S



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:44069 CAPLUS
DOCUMENT NUMBER: 132:251126
TITLE: Design and Synthesis of Piperazine-Based Matrix **Metalloproteinase** Inhibitors
AUTHOR(S): Cheng, Menyan; De, Biswanath; Pikul, Stanislaw; Almstead, Neil G.; Natchus, Michael G.; Anastasio, Melanie V.; McPhail, Sara J.; Snider, Catherine E.; Taiwo, Yetunde O.; Chen, Longyin; Dunaway, C. Michelle; Gu, Fei; Dowty, Martin E.; Mieling, Glen E.; Janusz, Michael J.; Wang-Weigand, Sherry
CORPORATE SOURCE: Health Care Research Center, Procter and Gamble Pharmaceuticals, Mason, OH, 45040, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(3), 369-380
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

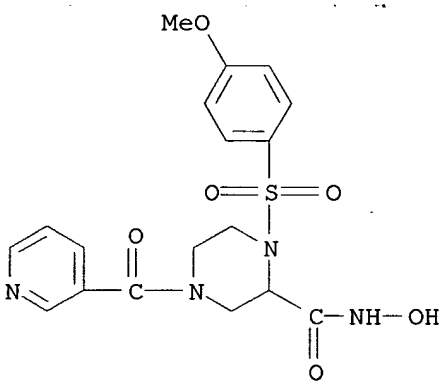
AB A new generation of cyclic matrix **metalloproteinase** (MMP) inhibitors derived from dl-piperazinecarboxylic acid was described. The design involves: incorporation of hydroxamic acid as the bidentate chelating agent for catalytic Zn2+, placement of a sulfonamide group at the 1N-position of the piperazine ring to fill the S1' pocket of the enzyme, and finally attachment of diverse functional groups at the 4N-position to optimize potency and peroral absorption. A unique combination of all three elements produced 3-[(hydroxyamino)carbonyl]-4-[(4-methoxyphenyl)sulfonyl]-1-piperazinecarboxylic acid phenylmethyl ester with high affinity for MMP-1, MMP-3, MMP-9, and MMP-13 (24, 18, 1.9, and

1.3 nM, resp.). X-ray crystallog. data obtained for MMP-3 co-crystd. with 3-[(hydroxyamino)carbonyl]-4-[(4-methoxyphenyl)sulfonyl]-1-piperazinecarboxylic acid phenylmethyl ester gave detailed information on key binding interactions defining an overall scaffold geometry for piperazine-based MMP inhibitors.

IT **262420-38-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and activity of N-hydroxy(phenylsulfonyl)piperazinecarboxamides as matrix **metalloproteinase** inhibitors)

RN 262420-38-2 CAPLUS

CN 2-Piperazinecarboxamide, N-hydroxy-1-[(4-methoxyphenyl)sulfonyl]-4-(3-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:498326 CAPLUS
DOCUMENT NUMBER: 129:148991
TITLE: Preparation of N-sulfamoylpiperidine-2-hydroxamic acids and analogs as **metalloproteinase** inhibitors
INVENTOR(S): Broka, Chris Allen; Campbell, Jeffrey Allen; Castelhano, Arlindo Lucas; Chen, Jian Jeffrey; Hendricks, Robert Than; Melnick, Michael Joseph; Walker, Keith Adrian Murray
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.; Agouron Pharmaceuticals, Inc.
SOURCE: Ger. Offen., 84 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19802350	A1	19980730	DE 1998-19802350	19980122
WO 9832748	A1	19980730	WO 1998-EP180	19980114

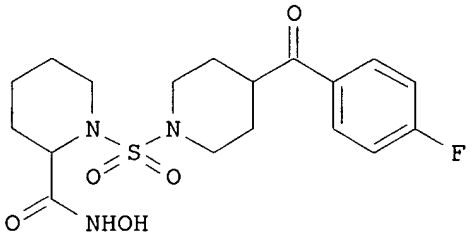
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9866140	A1	19980818	AU 1998-66140	19980114	
AU 730127	B2	20010222			
EP 958287	A1	19991124	EP 1998-907943	19980114	
EP 958287	B1	20020911			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 9807508	A	20000321	BR 1998-7508	19980114	
NZ 336625	A	20010427	NZ 1998-336625	19980114	
JP 2001523222	T2	20011120	JP 1998-531537	19980114	
AT 223909	E	20020915	AT 1998-907943	19980114	
CN 1093125	B	20021023	CN 1998-803233	19980114	
ZA 9800376	A	19980723	ZA 1998-376	19980116	
IT 1298163	B1	19991220	IT 1998-MI91	19980120	
FR 2758559	A1	19980724	FR 1998-601	19980121	
GB 2321641	A1	19980805	GB 1998-1393	19980122	
GB 2321641	B2	20010401			
ES 2136037	A1	19991101	ES 1998-113	19980122	
ES 2136037	B1	20001116			
NO 9903587	A	19990922	NO 1999-3587	19990722	
MX 9906822	A	20000131	MX 1999-6822	19990722	

PRIORITY APPLN. INFO.:	US 1997-36714P	P	19970123
	US 1997-62209P	P	19971016
	WO 1998-EP180	W	19980114

OTHER SOURCE(S): MARPAT 129:148991

GI



II

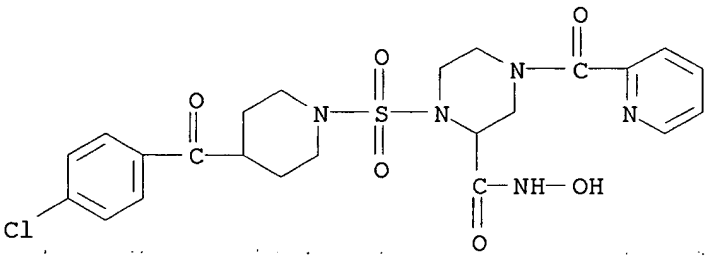
AB R10COCR1R2NR3SO2NR20R21 [I; R1-R3 = H, (CO-interrupted) alkyl, heterocyclyl(alkyl), (hetero)aryl(alkyl), etc.; R1R2, R1R3, R2R3 = atoms to complete a ring; R10 = NR11OR12; R11,R12 = H or (ar)alkyl; R20,R21 = H, alkyl, (hetero)aryl[alk(en)yl], etc.; NR20R21heterocyclyl] were prepd. Thus, (R)-1-[4-(4-chlorobenzoyl)piperidine-1-sulfonyl]piperidine-2-carboxylic acid was amidated by H2NOCMe3 and the product deprotected to give title compd. (R)-II. Data for biol. activity of I were given.

IT **210915-42-7P 210916-04-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-sulfamoylpiperidine-2-hydroxamic acids and analogs as **metalloproteinase** inhibitors)

RN 210915-42-7 CAPLUS

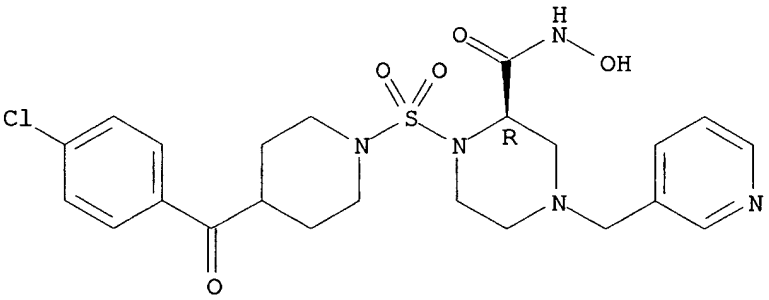
CN 2-Piperazinecarboxamide, 1-[[4-(4-chlorobenzoyl)-1-piperidinyl]sulfonyl]-N-hydroxy-4-(2-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



RN 210916-04-4 CAPLUS

CN 2-Piperazinecarboxamide, 1-[[4-(4-chlorobenzoyl)-1-piperidinyl]sulfonyl]-N-hydroxy-4-(3-pyridinylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:424232 CAPLUS

DOCUMENT NUMBER: 129:95510

TITLE: Preparation of 2-piperazinecarboxamides as inhibitors of MMP or TNF

INVENTOR(S): Neya, Masahiro; Yamazaki, Hitoshi; Kayakiri, Natsuko; Sato, Kentaro; Oku, Teruo

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan; Neya, Masahiro; Yamazaki, Hitoshi; Kayakiri, Natsuko; Sato, Kentaro; Oku, Teruo

SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

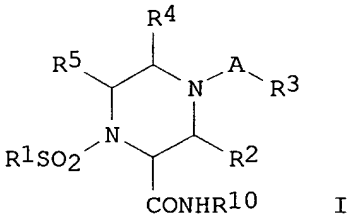
WO 9827069	A1	19980625	WO 1997-JP4613	19971215	
W: AU, CA, CN, HU, IL, JP, KR, MX, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
ZA 9711284	A	19980623	ZA 1997-11284	19971215	
AU 9854122	A1	19980715	AU 1998-54122	19971215	
EP 948489	A1	19991013	EP 1997-947944	19971215	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 2001506257	T2	20010515	JP 1998-527536	19971215	
KR 2000057595	A	20000925	KR 1999-705374	19990615	
US 6333324	B1	20011225	US 1999-319928	19990726	
US 2002128270	A1	20020912	US 2001-982869	20011022	
US 6489324	B2	20021203			

PRIORITY APPLN. INFO.:

AU 1996-4249	A	19961217
AU 1997-7156	A	19970603
AU 1997-8568	A	19970814
WO 1997-JP4613	W	19971215
US 1999-319928	A3	19990726

OTHER SOURCE(S): MARPAT 129:95510

GI



I

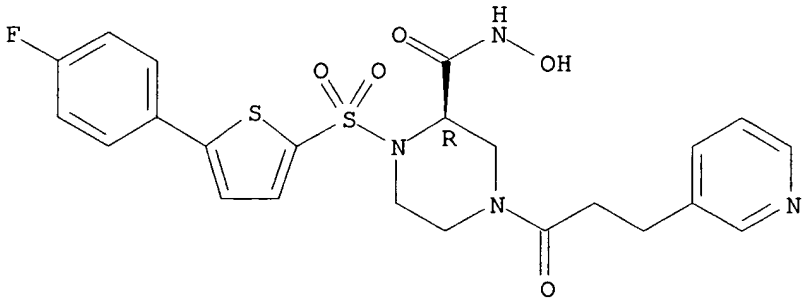
AB The title compds. [I; A = SO2, C(O); R1 = (un)substituted aryl, heterocyclic, lower alkyl, lower alkenyl; R2 = H, (un)substituted lower alkyl, aryl, heterocyclic; R3 = (un)substituted lower alkyl, lower alkoxy, aryloxy, etc.; R4 = H, (un)substituted lower alkyl, aryl, heterocyclic; R5 = H, (un)substituted lower alkyl, aryl, heterocyclic; R10 = OH, protected OH] and their pharmaceutically acceptable salts, useful for prophylactic and therapeutic treatment of MMP- or TNF.alpha.-mediated diseases, were prepd. Thus, treatment of a soln. of (2R)-1-(4-nitrobenzenesulfonyl)-4-methanesulfonylpiperazine-2-[N-(2-tetrahydropyranyloxy)]carboxamide in MeOH with 10% HCl-MeOH afforded (2R)-I [R1 = 4-O2NC6H4SO2; R2 = R4 = R5 = H; R3 = Me; R10 = OH] which showed 95.3% inhibition of collagenase activity at 1x10-6 M.

IT **209590-20-5P 209590-22-7P 209591-56-0P 209591-57-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-piperazinecarboxamides as inhibitors of MMP or TNF)

RN 209590-20-5 CAPLUS

CN 2-Piperazinecarboxamide, 1-[[5-(4-fluorophenyl)-2-thienyl]sulfonyl]-N-hydroxy-4-[1-oxo-3-(3-pyridinyl)propyl]-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

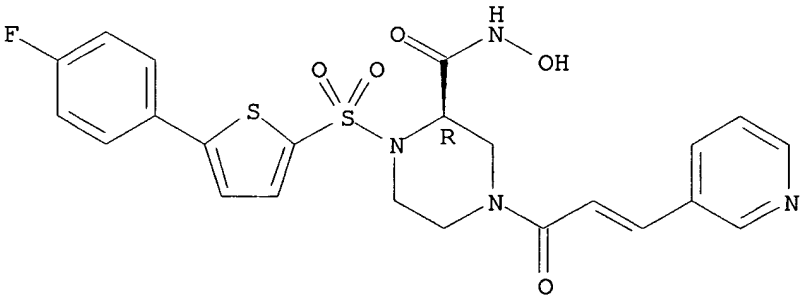
Absolute stereochemistry.



● HCl

RN 209590-22-7 CAPLUS
CN 2-Piperazinecarboxamide, 1-[[5-(4-fluorophenyl)-2-thienyl]sulfonyl]-N-hydroxy-4-[1-oxo-3-(3-pyridinyl)-2-propenyl]-, monohydrochloride, (2R)-(9CI) (CA INDEX NAME)

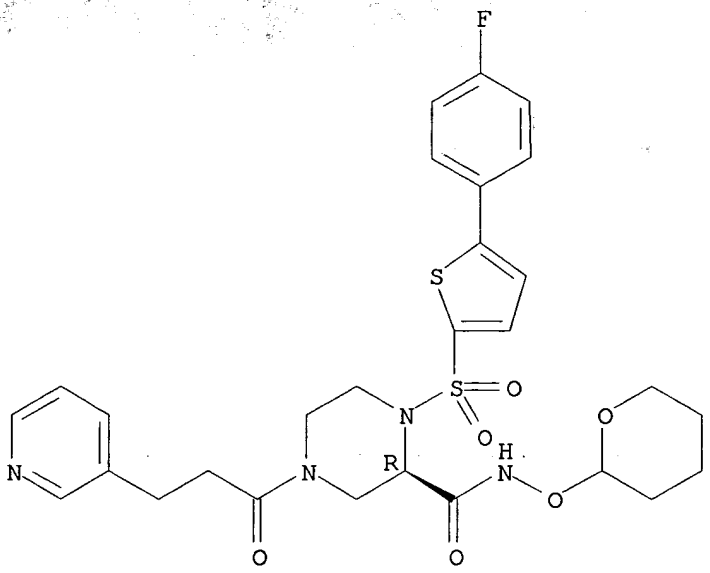
Absolute stereochemistry.
Double bond geometry unknown.



● HCl

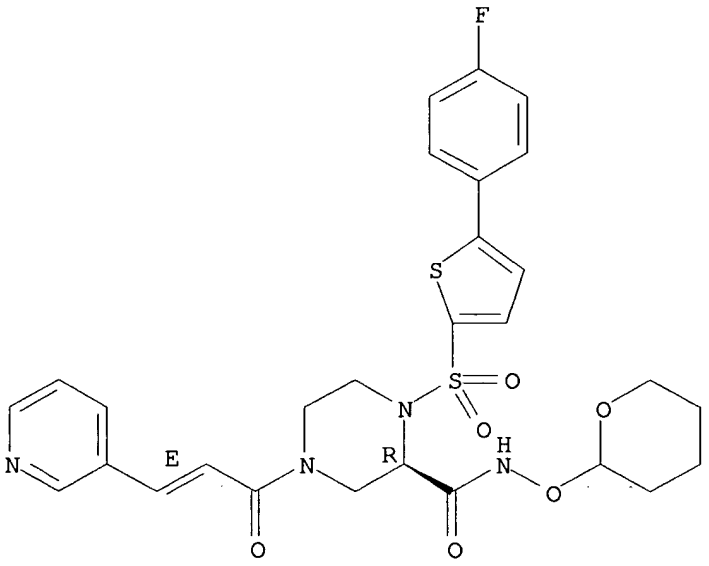
RN 209591-56-0 CAPLUS
CN 2-Piperazinecarboxamide, 1-[[5-(4-fluorophenyl)-2-thienyl]sulfonyl]-4-[1-oxo-3-(3-pyridinyl)propyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 209591-57-1 CAPLUS
CN 2-Piperazinecarboxamide, 1-[[5-(4-fluorophenyl)-2-thienyl]sulfonyl]-4-[(2E)-1-oxo-3-(3-pyridinyl)-2-propenyl]-N-[(tetrahydro-2H-pyran-2-yl)oxy]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	70.60	218.96

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.77	-9.77

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